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Amendments to the Specification:

On page 6, please replace the third full paragraph with the rewritten paragraph provided herewith.

> --In a tenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, this method includes creating a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside.--

At the bottom of page 6 going over to page 7, please replace the paragraph traversing these pages with the following rewritten paragraph.

> -- In a eleventh aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG

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dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, CpG-containing oligonucleotides according to this aspect of the invention include a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside.--

On page 7, replace the first full paragraph with the following rewritten paragraph.

-- In an twelfth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 3'-substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, CpG-containing oligonucleotides used in this aspect of the invention include a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside. --

On page 7 going onto page 8, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

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--In a thirteenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 8, please replace the first full paragraph with the following rewritten paragraph.

-- In a fourteenth aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising an uncharged internucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. --

On page 8 going onto page 9, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

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-- In a fifteenth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 9, please replace the first full paragraph with the following rewritten paragraph.

-- In a sixteenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 9, please replace the last paragraph with the following rewritten paragraph.

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-- In a seventeenth aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. --

On page 10, please replace the only paragraph on this page with the following rewritten paragraph.

-- In an eighteenth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

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On page 19 going onto page 20, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

-- In a tenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, this method includes creating a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside. --

On page 20, please replace the second full paragraph with the following rewritten paragraph.

-- The method according to this aspect of the invention can be conveniently carried out using any of the well-known synthesis techniques by simply using the appropriate 3' substituted monomer synthon in the synthesis process in the cycle immediately following the incorporation of the CpG dinucleotide. Preferred monomers include phosphoramidites, phosphotriesters and H-phosphonates. Thus, for purposes of the invention, "introducing into the oligonucleotide a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd

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nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof" simply means synthesizing an oligonucleotide that has a 3' substituted nucleoside at such a position or positions. --

On page 20 going onto page 21, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

-- In a eleventh aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising a 3' substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, CpG-containing oligonucleotides according to this aspect of the invention include a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside. --

On page 21 going onto page 22, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

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-- In a twelfth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 3'-substituted nucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. In preferred embodiments, CpG-containing oligonucleotides used in this aspect of the invention include a 2'-5' linkage between the 2' position of a 3' substituted nucleoside and the 5' position of another nucleoside, which may or may not be a 3' substituted nucleoside. --

On page 23, please replace the last full paragraph with the following rewritten paragraph.

-- In a thirteenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain

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preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 24 going onto page 25, please replace the paragraph that traverses these two pages with the following rewritten paragraph.

-- In a fourteenth aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising an uncharged internucleoside at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. Preferred oligonucleotides according to this aspect of the invention are complementary to a gene or gene transcript. More preferably, such oligonucleotides have antisense activity. In some preferred embodiments, the oligonucleotide has only one uncharged internucleoside linkage for each CpG dinucleotide present in the oligonucleotide. In some preferred embodiments, the oligonucleotide has only one an uncharged internucleoside linkage. --

On page 25, please replace the second full paragraph with the following rewritten paragraph.

-- In a fifteenth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising an uncharged internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG

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dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 26 going on to page 27, please replace the paragraph that traverses these pages with the following rewritten paragraph.

-- In a sixteenth aspect, the invention provides a method for increasing the immunostimulatory effect of a CpG-containing oligonucleotide. The method according to this aspect of the invention comprises introducing into the oligonucleotide a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --

On page 27 going on to page 28, please replace the paragraph that traverses these pages with the following rewritten paragraph.

-- In a seventeenth aspect, the invention provides CpG-containing oligonucleotides having increased immunostimulatory effects, the oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG

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dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. --

On page 28, please replace the second full paragraph with the following rewritten paragraph.

-- In an eighteenth aspect, the invention provides a method for inducing an immune response in a mammal, the method comprising administering to the mammal an oligonucleotide comprising a 2'-5' internucleoside linkage at a position selected from the group consisting of 3rd nucleoside 5' to the CpG dinucleotide, 4th nucleoside 5' to the CpG dinucleotide, 5th nucleoside 5' to the CpG dinucleotide, 6th nucleoside 5' to the CpG dinucleotide, 2nd nucleoside 3' to the CpG dinucleotide, 3rd nucleoside 3' to the CpG dinucleotide, 4th nucleoside 3' to the CpG dinucleotide, 5th nucleoside 3' to the CpG dinucleotide, 6th nucleoside 3' to the CpG dinucleotide, ~~7th nucleoside 3' to the CpG dinucleotide, 8th nucleoside 3' to the CpG dinucleotide, 9th nucleoside 3' to the CpG dinucleotide, 10th nucleoside 3' to the CpG dinucleotide,~~ and combinations thereof. In certain preferred embodiments, the oligonucleotide is not an antisense oligonucleotide. --